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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/205,658	12/03/98	RUVKUN G	00786/351004

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EXAMINER	
KAUSHAL, S	
ART UNIT	**PAPER NUMBER**
1633	15

DATE MAILED: 07/27/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
09/205,658	RUVKUN et al
Examiner	**Group Art Unit**
SUMESH KAUSHAL	1633

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☐ expires _____ months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on *Jul 14, 2000* (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on *Jan 10, 2000* has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☐ Applicant's response has overcome the following rejection(s):

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☐ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: *1-5, 8-23, 25, and 26 for the same reasons of record.*

☐ The proposed drawing correction filed on _____ ☐ has ☐ has not been approved by the Examiner.

☒ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). *11* .

☒ Other *see attachment.*

Attachment to Advisory Action.

Claims 1-5, 8-23 and 25-26 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, and is repeated for the same reasons as set forth in the official action mailed 01/10/00.

The claims when read in the light of specification, embrace the identification of compounds that are capable of ameliorating or delaying the onset of impaired glucose intolerance, obesity and/or increasing longevity in all animals, including mammals by monitoring the expression/activity of human PTEN.

Applicant's arguments filed 07/14/00 have been fully considered but they are not persuasive. The applicant argues that human PTEN (DAF-18) can be cloned and characterized by routine methodology. However, this is not found persuasive because identification of regulatory regions in mammalian PTEN gene is germane to the instant invention. The invention requires the making and using of genetically engineered cells and/or transgenic nematodes, wherein the compounds are identified that increases the expression of mammalian PTEN transgene. Furthermore, the genetic interaction among various DAF genes is complex and is only well studied in C. elegans (Larsan et al, Genetics 139:1567-1583, 1995). Therefore, the claimed method for identification of the compounds that involved putative mammalian DAF transgenes would not only be highly unpredictable in case of C.elegans but also in other transgenic nematodes.

The applicant argues that the specification is enabled for making a transgenic C. elegans expressing def-18 or human PTEN. This is not found persuasive because the transgenic DAF-18

nematode is a mutant C. elegans (e1375) encoding a mutation in DAF-18 gene and therefore is not a transgenic nematode by recombinant means.

The applicant argues that the mammalian PTEN expression and activity regulate both impaired glucose tolerance, obesity and/or longevity in all animals. The applicant further argues that a 14 year old diabetic insulin-resistant patient, who is morbidly obese carried the same insulin receptor mutation as the DAF-2 C.elegans mutant (e1391). However, this is not found persuasive because applicant fails to disclose a DAF-18 mammalian homolog, wherein the disruption of such homolog results in the impaired glucose tolerance, obesity and/or increase in longevity. Therefore, without clear correlation that the mammalian DAF-18 gene results in impaired glucose tolerance, and is associated with longevity or the onset obesity, it is unclear how the claimed method can identify compounds for the amelioration of such effects or diseases in mammals.

Thus, in view of the lack of guidance in the specification and unpredictability in the art, the skilled artisan at the time of filing would have had to engage in undue experimentation to identify agents for the treatment of impaired glucose tolerance, obesity and/or increase in longevity related to DAF-18 (PTEN) expression. The quantity of experimentation required would have included the characterization of mammalian DAF-18 signaling pathway and its role in the onset of impaired glucose tolerance, longevity or obesity and correlation, if any of the mutant C.elegans as an appropriate model for the related situation in mammals.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor John L. LeGuyader can

be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-2035. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

S. Kaushal, AU 1633

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